*Case Report*

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# Multiple Co-Infections in a Child with Beta Thalassemia Major: A Rare Case Report

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**Abstract**

Beta Thalassemia is a hereditary blood disorder characterized by defect in synthesis of beta chains of haemoglobin requiring regular blood transfusion and chelation therapy. Blood transfusions can lead to many complications of which transfusion transmitted infections like HCV, HBsAg, HIV etc are possible. Iron overload is another complication of repeated blood transfusion which further predisposes them to many infections like Mycobacterium Tuberculosis. Hemophagocytic Lymphohistiocytosis (HLH) is one of the rare complication where there is abnormal activation of immune system which results in cytokine storm. Here we present a case of transfusion dependent thalassemia patient, who developed HCV and Pulmonary Kochs complicated with HLH all at the same time and was managed successfully.

**Keywords:** Thalassemia; HCV; Tuberculosis; HLH.

## INTRODUCTION

β-thalassemia major is an autosomal recessive disorder requiring regular blood transfusion and chelation therapy.[1] Infection is one of the cause of morbidity and mortality in thalassemia patient. The underlying mechanism of increased susceptibility to infections is specific to unscreened blood transfusion, iron overload, splenectomy, chelation therapy.

The implementation of viral NAT testing has significantly reduced the risk of viral transmission through blood products during the window period.[2,3] However, these infections still can occur in settings of developing countries where blood is poorly screened with old techniques.

Regular transfusions leads to iron overload in various organs leading to organ dysfunction. It also increases the predisposition to infections including TB. Adequate chelation therapy is required to prevent and reduce susceptibility to infections.[4,5]

Hemophagocytic lymphohistiocytosis (HLH) is a rare, potentially fatal condition in which abnormal activation of the immune system results in hemophagocytosis, inflammation and tissue damage. HLH can be either primary (familial) or secondary (sporadic, acquired). Secondary HLH can occur secondary to many infections, including Mycobacterium tuberculosis (MTB).

These illnesses have high morbidity and mortality individually which can increase significantly when combined together. Early diagnosis and timely intervention is the key to managing such a child.

## CASE REPORT

13 year old male child, a known case of Transfusion Dependent B Thalassemia was

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following up regularly for blood transfusion and chelation therapy at our centre. Child was monitored regularly for transfusion transmitted infections as per protocol and was negative for HIV, HCV, HBSAG, etc. During the pandemic of covid, the patient shifted to his village and took transfusions there. Chelation therapy was discontinued due to unavailability of the drugs for 9 months.

The child presented to us with complaints of high grade fever without focus since 3 days. On examination, the child was sick looking and had tachycardia. He had generalized lymphadenopathy with stunting and wasting on anthropometric measurements. The abdomen was distended with massive hepatomegaly (span 22cm). The child was splenectomised 5 years back for hypersplenism. His CBC showed Hb of 11 gm/dl, TLC-13600 cells/cumm, Platelet - 3 lakhs, ESR was elevated (85 mm at end of 1 hr). Serum Ferritin was 69750 ng/ml.(7140ng/ml), electrolytes were normal. Serological tests for Malaria, Dengue and Typhoid were negative. Covid-19 RTPCR was negative, Blood culture was negative, urine was sterile. On screening, he was detected to have developed anti HCV antibodies.

Patient was started on IV Ceftriaxone, even after 48hours of antibiotics, patient had high grade fever & persistent vomiting and developed hypotension, so antibiotics were stepped up to Meropenem and Vancomycin. Patien was shifted to PICU. Serum electrolytes showed severe hyponatremia (Na+- 121) and hypokalemia (K+ -3.2) and correction fluids were started. Patient developed ascites, episodes of desaturation and hypotension persisted so oxygen and inotropic support was given. X ray chest showed findings suggestive of Koch's. Hence was further worked up by doing HRCT chest which showed enlarged pre and para tracheal, sub carinal and multiple mediastinal lymphnodes with calcification which were consistent with Kochs, however however MT (MantouxTest) and Gene expert were negative. FNAC of lymph nodes was done which was inconclusive due to scanty cellularity. AKT was started as per RNTCP DOTS. Repeat CBC showed pancytopenia along with persistent fever, so HLH work up was done. Serum triglycerides, soluble cd25 and fibrinogen were normal. On strong suspicion Bone Marrow aspiration and Biopsy was done which was suggestive of hemophagocytosis. Patient was started on dexamethasone @10mg/m2 as per HLH protocol

The child showed gradual improvement with reduction of fever, inotropic support and oxygen requirement and normalization of electrolytes. Child was started on oral feeds. Chelation therapy was restarted and serum Ferritin was repeated, which came down to 16,072 ng/ml. As patient was hemodynamically stable, he was shifted to oral dexamethasone and referred to gastroenterologist for further management of HCV and advised to complete the AKT treatment.

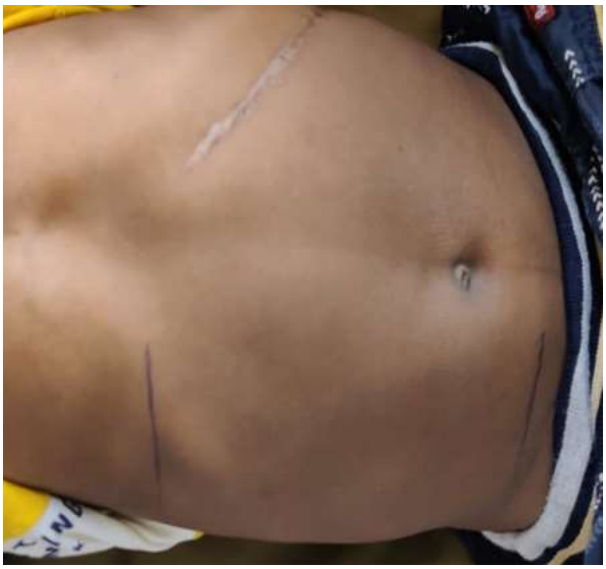

**Fig 1:** Photograph showing the massive Liver on the right side of the body and splenectomy scar on left side of the body.

## DISCUSSION

Beta Thalassemia patients receive regular blood transfusion which results in Iron over load. Iron and its binding proteins has immunoregulatory properties. Iron excess may derange the immune balance in favour of the growth of infectious organisms. Other factors which increase susceptibility to infections include multiple transfusions increasing risk of Transfusion transmitted infections and splenectomy.[6] Our patient was on regular blood transfusion with irregular chelation with massive hepatomegaly and was splenectomised, which resulted in immuno compromised state.

Tuberculosis is an opportunistic infection having non-specific nature of symptoms making diagnosis difficult. Immunocom promised state increases the risk of Tuberculosis[(7)]. Combination of clinical, radiological, lab findings and epidemiological evidence of TB exposure allows for an accurate diagnosis. A study by Sriwijitali et al showed a common pathway via glutathione which imply the

increased risk for tuberculosis among the patients with thalassemia.[8]

HLH is characterised by persistent fever with hepatomegaly, splenomegaly, lymphadenopathy, cytopenia, hypertriglyceridemia, hypofibrinogenemia and bleeding.[9] There is stimulation of immune responses which results in macrophage infiltration and cytokinestorm.[10] The excessive activated macrophages engulf host blood cells (hemophagocytosis) which can be seen in biopsies from lymph nodes, bone marrow, liver and spleen. Secondary HLH can be triggered by infections, most commonly viral infections like EBV, CMV, HCV, HBV, Dengue, etc and also with fungal, parasitic and bacterial infections, including Mycobacterium tuberculosis (TB). Timely diagnosis and initiation of treatment is an important factor in prognostication. Study conducted by Zhang et al showed around 3.5% prevalence of HLH in Tuberculosis patient.[11]

Due to covid pandemic and unavailability of drugs, our patient was not on regular chelation therapy and received unscreened blood transfusion and developed HCV infection. Most patients of hepatitis C have non-specific symptoms during acute phase. The severity of liver fibrosis correlates to liver iron over load in chronic hepatitis C. Manifestations in patients with decompensated liver disease include ankle oedema, abdominal distension (ascites), hematemesis or melena (variceal bleeding) with abnormal liver function tests and mental status changes (hepatic encephalopathy).[12] Study conducted by Thalassaemia Control Unit, Imambara Sadar Hospital showed 25% prevalence of HCV in thalassemia patient.[13]

Even though complications of Hep C infection, Tb and HLH can occur in a thalassemia patient, all these occurring together complicating a case of thalassemia is rarely seen. Early diagnosis and recognition of complications helped us in managing the case successfully.

## CONCLUSION

HCV infection can occur in thalassemia due to inadequate screening technique or window period. TB is an endemic illness in India, more common in immunocompromised conditions such as splenectomised thalassemia child. In a child with persistent fever with pancytopenia, diagnosis of HLH should be considered early as prompt diagnosis and treatment can be life saving.

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